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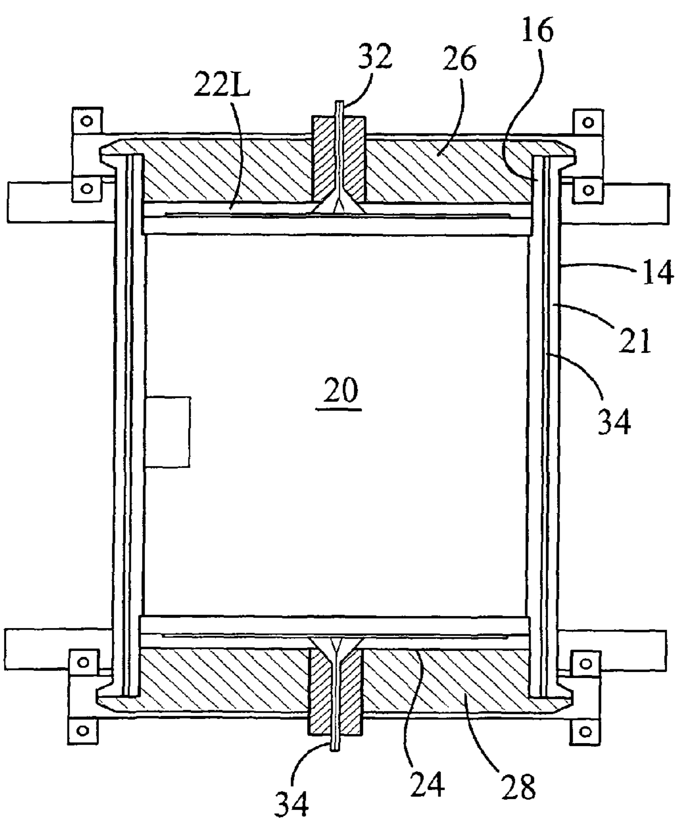
(54) Title: APPARATUS AND METHOD FOR PURIFYING A CHEMICAL CONTAINED IN A SOLUTION



(57) Abstract: Purifying a chemical contained in a solution using a cylindrical cartridge (16) that contains tightly packed activated carbon powder (20) and has flexible walls (21) that transmit externally applied pressure to the interior. The solution being treated is supplied under pressure to cartridge (16), while externally applied pressure is applied to the flexible walls (21), and purified solution is removed from the outlet (34).

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IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

APPARATUS AND METHOD FOR PURIFYING A CHEMICAL CONTAINED IN A SOLUTION

BACKGROUND

The invention relates to purifying chemicals contained in solution.

Pharmaceuticals are subject to extremely high standards of purity and safety. Unfortunately, even the most refined processes may contain unwanted side products. Often these impurities will cause discoloration affecting the aesthetic and real value of the final substance. Color is a trace impurity that remains with the product of interest after single or multiple purification steps. Color can be a starting material, a reaction byproduct, an oxidized form of the product, or a totally independent molecule. In most pharmaceutical applications, the color is removed prior to crystallization, often by batch adsorption with powdered activated carbon. Activated carbon has also been used in a broad range of other pharmaceutical purification applications including purifying fermentation products, pyrogen removal, amino acid production, removing catalysts and organic synthesis purification. Batch processing typically requires multiple particulate filtration steps to remove the particles from the purified solution. However, handling the fine particles in powdered activated carbon complicates the process. Cleaning the equipment after the batch adsorption process can involve significant labor and safety issues.

Flow-through columns containing activated carbon have also been used to purify pharmaceuticals. Granular activated carbon is typically selected to improve flow rate. This provides a limited surface area and a poorly packed bed with many channels. The channels permit early breakthrough, and require repeated passes through the column to get maximum use from the carbon. The columns are typically manually cleaned and repacked with fresh granular between uses.

SUMMARY

The invention features, in general, purifying a chemical contained in a solution by passing it through a tightly packed bed of activated carbon particles contained in a

flexible walled cylinder. The cylinder is contained in a pressure chamber that exerts pressure through the flexible walls to the bed therein.

In one aspect the invention relates to a disposable, flexible-walled cartridge containing tightly packed activated carbon for use in a pressurized chamber. In other aspects, the invention features apparatus including the cartridge in the pressurized chamber and the method of purifying liquid by passing it through a flexible-walled cartridge in the pressurized chamber.

Particular embodiments of the invention may include one or more of the following features. The activated carbon is packed to have a void volume less than 80 %, preferably less than 75%. The cylinder and activated carbon provide a column having a plate count of greater than 100, preferably greater than 400 plates per meter. The activated carbon powder has a majority of particles having a particle size less than 100 microns, preferably between 20 and 60 microns. The solution to be treated flows through the cylinder with a linear velocity greater than 800 cm/hr, preferably greater than 1000 cm/hr.

Embodiments of the invention may include one or more of the following advantages. The apparatus provides fast, thorough purification, and efficiently uses the active sites on the activated carbon with a short breakthrough period. The rate that the crude solution can be pumped through the cartridge is very high. In addition the total volume of solution processed before the carbon is saturated and breakthrough is a much greater volume. Because the cartridges are disposable, new carbon can be replaced without difficulty and without handling loose powder. Used cartridges can be removed and safely disposed of as a unit. Use of cartridges reduces operator exposure to solvents, contaminants, active ingredients, and loose activated carbon powder. Throughout the purification process, activated carbon powder remains fixed in place. The system does not require extensive process time or cleaning after each batch. The pre-packed cartridges can also be used in parallel, to achieve a continuous purification process. In this approach, a new cartridge can be brought on-line as the previous cartridge is exhausted.

Other advantages and features of the invention will be apparent from the following description of a particular embodiment thereof and from the claims.

DESCRIPTION OF DRAWINGS

Figure 1 is a diagram of an apparatus for purifying a chemical.

Figure 2 is a partial sectional view of a pressure chamber and disposable cartridge of the Figure 1 apparatus.

Figure 3 is an enlarged, diagrammatic, partial sectional view showing the walls of the Figure 2 chamber and cartridge.

DETAILED DESCRIPTION

Description of a Particular Embodiment

Referring to Figure 1, there is shown apparatus for purifying chemicals 10. The apparatus includes compression reservoir 12, compression chamber 14, disposable cartridge 16 therein, and valve as a fraction collection device 18.

Referring to Figure 2, it is seen that cartridge 16 includes packed activated carbon particles 20 in flexible walled cylinder 21 between inlet manifold 22 and outlet manifold 24. Cylinder 21 is made of plastic, e.g., polyethylene. Chamber 14 includes top plate 26 and bottom plate 28, which are sealed to the sidewalls 30 of chamber 14. There also is a liquid tight seal between the inflow line 32 in the inlet manifold 22 and another liquid tight seal between outlet line 34 and outlet manifold 24. A source of pressurized fluid (liquid or gas) is connected to the region 36 between flexible wall 21 and wall 30 of the pressure chamber. The pressurized liquid provides radial compression to flexible wall 21 in a manner similar to the application of radial compression to chromatography cartridges having flexible walls, as described in U.S. Patents Nos. 4,250,035 and 5,601,708 and PCT Published Applications Nos. WO97/43024 and WO99/25451, which are hereby incorporated by reference.

The majority of particles of activated carbon 20 have a particle size less than 100 microns, and preferably have a particle size between 20 and 60 microns. The activated carbon is peat based and steam activated. Other activated carbon based on wood, coal or coconut husks and activated by other means, e.g., acid, can also be employed. Activated carbon powder 20 is tightly packed within cylinder wall 21 so as to provide a void volume of 80% or less, preferably 75% or less.

In operation, the chemical to be purified is contained in a solution that is fed from compression reservoir 12 under pressure and at a relatively high flow rate through cartridge 16, given the small particle size and small void volume. The solution is

supplied at a pressure between 20 psi and 100 psi or higher. The pressure in chamber 14 is maintained at least 20 psi greater than the pressure of the solution passing through the cartridge 16. The flow rate of the solution depends on the radius and bed depth of the cylinder and the applied solution pressure. In general, the flow rate is such as to provide a linear velocity through the cartridge of 800 cm/hr, preferably greater than 1000 cm/hr. As the colored solution is fed into a cartridge, it is forced through the packed bed, and exits as a color-free solution. Carbon is held stationary inside the cartridge, and no loose activated carbon powder enters the final solution.

As diagrammatically illustrated in Figure 3, the pressure is transmitted through flexible wall 21 to the particles of activated carbon 20 and tends to maintain a tightly packed bed. The effluent passes through line 34 to fraction collector 18 (Figure 1). The effluent is free of color or other contaminants while there still are active sites on the carbon, i.e., up until the carbon is exhausted. The cartridge thus desirably has a very long breakthrough volume and, when used at high flow rates, a short process time. It thus is easy to identify when a cartridge has been exhausted so that a new cartridge can be added.

The uniformity of particle packing and high density promote a high number of theoretical "plates," a parameter often used in chromatography column analysis. In general, the number of plates is representative of the number of times that a typical molecule reaches an equilibrium concentration absorbed onto the surface versus the local concentration in solution. Plate counts are based on the current definition provided by the USP. Columns with granular materials may have plate counts on the order of 8 plates per meter, while cartridge 16 with tightly packed carbon particles and radial compression can have over 100 plates per meter, preferably 400 to 500 plates or more. The greater the number of equilibrium stages, or plates, the greater the adsorbent capacity of the carbon is used before the cartridge is exhausted.

This higher capacity means the process can use less activated carbon to achieve the same result. Conversely, the same amount of carbon can be used for a much greater volume of crude solution.

The short breakthrough period allows carbon to be used to its maximum capacity before the adsorbent property of carbon is exhausted. Consistent performance is created by standardized packing technique across many sizes of columns that make

the system easy to scale up for larger processes. The scale up with this system is done simply by projecting at constant ratios of carbon mass to product mass.

Cartridge 16 removes the color and other contaminants in a single pass (columns with granular activated carbon can require multiple passes) and generally does so much faster than batch processes or granular columns. For example, cartridge 16 could process in twenty minutes a volume quantity of 9-fluorenylmethanol that would take nine hours in a batch process with an identical mass of carbon. Since the batch process is by definition a single equilibrium step, the time required to reach equilibrium is critical. Reducing contact time will reduce the capacity of the carbon, and leave impurities in the liquid. Since a high efficiency cartridge is equivalent to multiple batch adsorption steps, there are multitudes of activated carbon sites to bind impurities, even at high flow rates.

Because cartridges 16 are disposable, new carbon can be replaced without difficulty and without handling loose powder. Used cartridges can be removed and safely disposed of as a unit. The use of disposable cartridges reduces operator exposure to solvents, contaminants, active ingredients, and loose activated carbon powder. Throughout the purification process, activated carbon powder remains fixed in place. The system does not require extensive process time or post-batch cleaning.

Other embodiments of the invention are within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. Apparatus for purifying a chemical contained in a solution comprising

a pressure chamber for connection to a source of pressurized fluid,

a cylinder having flexible walls that transmit externally applied pressure to the interior, said cylinder being located in said pressure chamber,

activated carbon powder that is tightly packed inside said cylinder,

inlet and outlet manifolds in said cylinder containing said activated carbon powder therein, and

a source of said solution under pressure connected to said inlet.

2. The apparatus of claim 1 wherein said activated carbon is packed to have a void volume less than 80 %.

3. The apparatus of claim 1 wherein said cylinder and activated carbon provide a column having a plate count of greater than 100.

4. The apparatus of claim 1 wherein said cylinder and activated carbon provide a column having a plate count of greater than 400.

5. The apparatus of claim 1 wherein said activated carbon powder has a majority of particles having a particle size less than 100 microns.

6. The apparatus of claim 1 wherein said activated carbon powder has a majority of particles having a particle size between 20 and 60 microns.

7. A disposable cartridge for purifying a chemical contained in a solution comprising

a cylinder having flexible walls that transmit externally applied pressure to the interior,

activated carbon powder that is tightly packed inside said cylinder,

inlet and outlet manifolds in said cylinder containing said activated carbon powder therein, and

a source of said solution under pressure connected to said inlet.

8. The cartridge of claim 7 wherein said activated carbon is packed to have a void volume less than 80%.

9. The cartridge of claim 7 wherein said cylinder and activated carbon provide a column having a plate count of greater than 100.

10. The cartridge of claim 7 wherein said cylinder and activated carbon provide a column having a plate count of greater than 400.

11. The cartridge of claim 7 wherein said activated carbon powder has a majority of particles having a particle size less than 100 microns.

12. The cartridge of claim 7 wherein said activated carbon powder has a majority of particles having a particle size between 20 and 60 microns.

13. A method of purifying a chemical contained in a solution comprising

providing a cylindrical cartridge having flexible walls that transmit externally applied pressure to the interior, activated carbon powder tightly packed inside said cartridge, and inlet and outlet manifolds in said cartridge containing said activated carbon powder therein,

supplying said solution under pressure to said inlet while externally applied pressure is applied to said flexible walls, and

removing purified solution from said outlet.

14. The method of claim 13 wherein said activated carbon is packed to have a void volume less than 80 percent.

15. The method of claim 13 wherein said cylinder and activated carbon provide a column having a plate count of greater than 100.

16. The method of claim 13 wherein said cylinder and activated carbon provide a column having a plate count of greater than 400.

17. The method of claim 13 wherein said activated carbon powder has a majority of particles having a particle size less than 100 microns.

18. The method of claim 13 wherein said activated carbon powder has a majority of particles having a particle size between 20 and 60 microns.

19. The method of claim 13 wherein said solution flows through said cylinder with a linear velocity greater than 800 cm/hr.

20. The method of claim 13 wherein said solution flows through said cylinder with a linear velocity greater than 1000cm/hr.

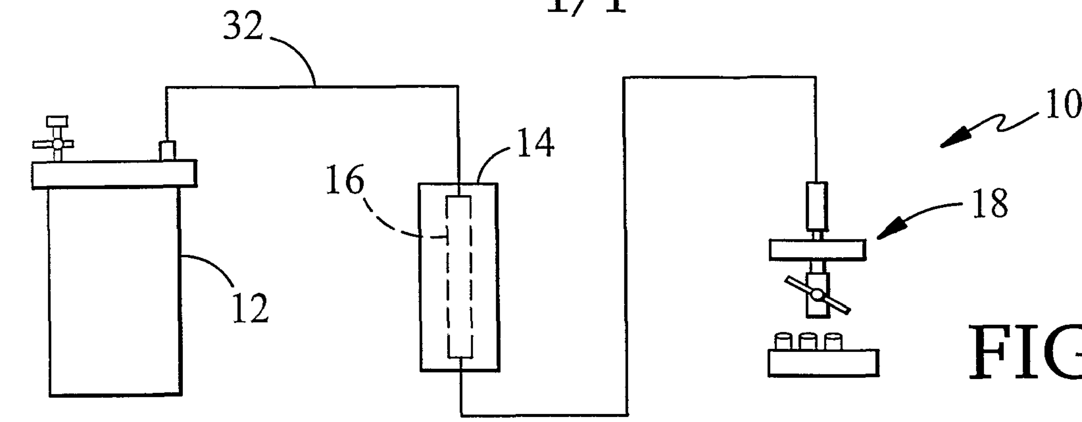

FIG. 1

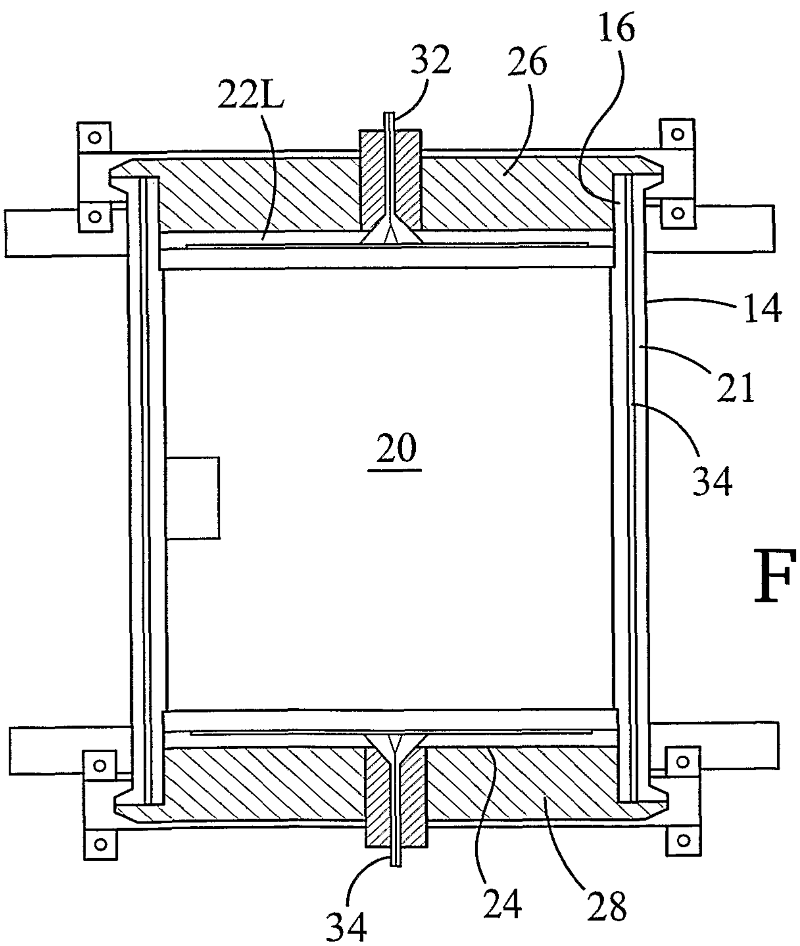

FIG. 2

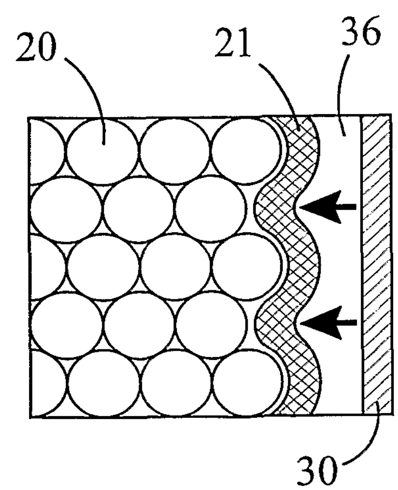

FIG. 3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/21956

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :B01D 15/00
US CL : 210/694, 282, 287, 351
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 210/694, 263, 282, 287, 350, 351

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 3,180,825 A (COUVREUR et al) 27 April 1965, entire document.	1-20
Y	US 5,904,854 A (SHMIDT et al) 18 May 1999, entire document.	1-20
A	US 3,965,000 A (MIKULE et al) 22 June 1976, entire document.	1-20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

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02 SEPTEMBER 2001	02 NOV 2001

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